DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
250 Marquette Ave, Ste. 600 Minneapolis, MN 55401 (612)334-4100 Fax:(612)334-4134	4/9/2019-4/23/2019* FEI NUMBER 3015213291

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
[redacted] Sponsor-Investigator

FIRM NAME	STREET ADDRESS
[redacted] Sponsor-Investigator	Hennepin County Medical Center, Dept Of Emergency Medicine, 701 Park Ave
CITY, STATE, ZIP CODE, COUNTRY Minneapolis, MN 55415-1623	TYPE ESTABLISHMENT INSPECTED sponsor-investigator

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

OBSERVATION 1

The sponsor failed to submit an IND to the FDA prior to conducting a clinical investigation with an investigational new drug.

Specifically, study [redacted] and [redacted] were conducted without submitting INDs.

OBSERVATION 2

Legally effective informed consent was not obtained from a subject or the subject's legally authorized representative, and the situation did not meet the criteria in 21 CFR 50.23 - 50.24 for exception.

Specifically, subjects were enrolled and treated on the following studies without obtaining informed consent, with neither study appearing to meet the criteria for exception from informed consent:

A. [redacted] - 747 subjects; and,

B. [redacted] - at least 874 subjects.

OBSERVATION 3

Not all changes in research activity were approved by an Institutional Review Board prior to implementation.

Specifically,

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	Sharon L Matson, Investigator	X Sharon L Matson Investigator Signed By: Sharon L. Matson -S Date Signed: 04-23-2019 13:11:52	4/23/2019

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A. For study [redacted]

1. Serious adverse events (SAEs) were not reported to the IRB as required by the IRB, e.g.:

Subject#	SAE
6	airway complication, required intubation
26	hypoxia, required nasal cannula oxygen
37	hypoxia, required nasal cannula oxygen, nasal/oral airway, and jaw thrust
300	hypoxia, required nasal cannula oxygen, face mask oxygen, and nasal/oral airway
346	hypoxia, required nasal cannula oxygen
498	airway complication, required intubation
594	pupils became pinpoint
619	hypoxia, required intubation
621	dystonia.

2. An additional treatment regimen was added to the study, using treatment Haloperidol at 10 mg from 9/21/2017 to 10/12/2017, without IRB review or approval.

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3. Seven-hundred and forty-seven (747) subjects in total were enrolled and treated on study a) over the 500 approved by the IRB, and b) over the 737 reported as the total enrollment to the IRB.

4. An IRB-required annual progress report was not submitted until about 6/29/2018, past the 5/22/2018 expiration of approval.

B. For study [redacted]

1. Serious adverse events (SAEs) were not reported to the IRB as required by the IRB, e.g.:

Subject#	SAE
35	akathisia
56	hypoxia, required nasal cannula oxygen
74	airway complication, required intubation
105	hypoxia
134	hypoxia
157	hypoxia
192	hypotension
197	hypoxia, required intubation.

2. A study change was submitted to the IRB and approved to voluntarily suspend study activities effective 7/16/2018, with a subsequent change submitted 11/5/2018 stating the study was closed. However, it appears the study continued with the same treatment regimen and data collection activities

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until at least the most recent enrollment of Subject 874 on 11/19/2018; and, the status of the study is posted on clinicaltrials.gov as "Recruiting". Changes in the study that do not appear to have been approved by the IRB include:

a) Continuing the study after the 7/16/2018 voluntary suspension submitted and approved;
b) Discontinuing provision of a Notification of Enrollment to subjects on about 7/16/2018; and,
c) Enrolling at least 874 subjects in total, over the 800 originally approved by the IRB.

3. An additional AMSS Data Validation sub-study was conducted without IRB review or approval.

OBSERVATION 4

An investigation was not conducted in accordance with the investigational plan.

Specifically, not all study conduct was in accordance with the study plans submitted to and approved by the IRB for [redacted] and [redacted], e.g.:

A. There is no documentation to show all subjects were provided a Notification of Enrollment form, e.g.:

1. [redacted] subject 1, 7, 9. 14, 15, 23, 46, 48, 161, 179, 197, 205, 299, 326, 332, 464, 511, 587, 593, 594, 607, 613, 631, and 633; and,

2. [redacted] subject 8, 9, 10, 66, 72, 136, 171, 172, 197, 205, 206, 208, 209, 213, 214, 215, 216, 217, and 874.

B. There is no documentation to show all Research Volunteers (RVs) that conducted study operations were trained, e.g.:

1. [redacted]

RV	conducted study operations with
ND	5, 8, 14, 173, 339, 343, 344

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MJ 304, 463, 502

ML 184, 189, 325, 490

HT 47; and,

2. [redacted]:

RV conducted study operations with

PD 175

HL 35

AK 40, 72

LD 178, 179, 184

EY 187, 190, 197.

OBSERVATION 5

Failure to prepare or maintain adequate and accurate case histories with respect to observations and data pertinent to the investigation and informed consent.

Specifically, for study [redacted] and [redacted]

there is no identification in source records to show who conducted:

A. screening, and completion of Screening Sheets for either study;

B. data collection from EMR, and completion of Chart Review form for either study; and,

C. data validation, and completion of the AMSS Data Validation form for study [redacted]

OBSERVATION 6

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Failure to ensure proper monitoring of the study.

Specifically, there is no documentation to show any monitoring of study [redacted] or [redacted]

OBSERVATION 7
Investigational drug disposition records are not adequate with respect to dates, quantity and use by subjects.

Specifically, no clinical investigator-required investigational drug disposition records were maintained for either study [redacted] or [redacted]

OBSERVATION 8
Lack of records covering receipt and disposition of an investigational drug.

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Specifically, no sponsor-required investigational drug records were maintained for either study [redacted] or [redacted]

***DATES OF INSPECTION**

4/09/2019(Tue), 4/10/2019(Wed), 4/11/2019(Thu), 4/15/2019(Mon), 4/16/2019(Tue), 4/17/2019(Wed), 4/18/2019(Thu), 4/23/2019(Tue)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or
2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration.

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgment, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."